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LETTERS TO THE EDITOR

Accuracy of OCT in Evaluating Neointimal Thickness After Stent Implantation

***Giuseppe Ferrante, MD, PhD**
Konstantinos Dimopoulos, MD, MSc, PhD
Rocco Antonio Montone, MD
Peter Barlis, MBBS, PhD

*Institute of Cardiology
Catholic University of the Sacred Heart
Largo Agostino Gemelli, 8
00168 Rome
Italy
E-mail: giu.ferrante@hotmail.it

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We read with great interest the article by Murata et al. (1), who compared the accuracy of optical coherence tomography (OCT) to histological analysis for the quantitative assessment of neointimal response after drug-eluting stent implantation in normal porcine coronary arteries. The authors should be commended for this study as the addressed issue is of clinical relevance, in view of the rapid widespread use of OCT in catheterization laboratories and the application of OCT end points in randomized clinical trials of intervention. Therefore, it is crucial to address the quantitative performance of OCT.

The authors conclude that OCT shows high correlation with histology for neointimal area, neointimal thickness, and luminal area measurement, but not for stent area assessment, based on squared correlation coefficient R^2 between values obtained by the 2 techniques of approximately 0.8 and 0.3 for high and poor correlation, respectively.

However, the validity of the results reported by Murata and colleagues must be interpreted with caution due to the type of statistical analysis used. When comparing 2 different techniques, the Pearson correlation coefficient (R), used in this study, is not appropriate and may be misleading (2). Indeed, a high correlation coefficient suggests a strong relation between 2 variables, but not necessarily a good agreement between 2 methods. On a scatterplot of values measured by 1 technique against another, agreement is present if points lie along the line of equality, whereas correlation is good when points lie along any straight line. Bland and Altman plots with estimation of limits of agreement and repeatability coefficients is the recommended approach when comparing 2 techniques or for the assessment of intraobserver and interobserver variability (2–4), and has been previously used in OCT studies of strut apposition and neointimal coverage (5). Therefore, further statistical verification of the agreement between OCT and histology in the measurement of neointimal response to stent implantation may be useful to confirm the results of the present, elegant study. Finally, the use of Student *t* test for the comparison of neointimal thickness may have resulted in falsely low (significant) p values, as *t* test assumes independence of observations, whereas struts belonging to a single stent are not independent. Multilevel analysis accounting for clustering of struts in stents, lesions, and/or subjects is an appropriate, albeit computationally demanding, approach.

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REPLY

We are glad to respond to the letter sent by Ferrante et al. and appreciate the time taken to review and comment on our article (1) comparing the accuracy of optical coherence tomography and histopathology in the assessment of the neointimal response following drug-eluting stent implantation in a preclinical model of coronary disease. It is important to highlight that the objective of our study was to compare the findings of data obtained in a clinically relevant fashion to histopathology findings. At first glance, the quantitative differences observed between all measured variables were minimal when both techniques were compared. In our study, regardless of the type of statistical methodology used, our findings suggested a high level of correlation between the 2 methods for the measurement of lumen areas, neointimal areas, and neointimal thicknesses. Although we are grateful for the comments regarding our statistical analysis methodology, we maintain our original position with regards to our paper's conclusions.

In particular, we agree that the inclusion of the fitted correlation line equation would elucidate the validity of our findings even further. Apart from the high R^2 values demonstrated between lumen areas, neointimal areas, and neointimal thicknesses measured by optical coherence tomography and histology, their points lie along a line very close to the line of equality in all measured parameters. As was stated, our analysis revealed a limited correlation between methodologies for the

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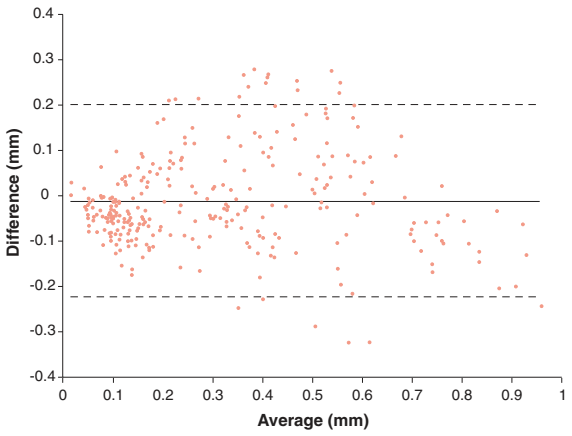

Figure 1. Bland-Altman Plot Demonstrating Similarity Between OCT and Histology in the Assessment of Neointimal Thickness

A Bland-Altman visualization of the differences between in vivo optical coherence tomography (OCT) and processed histology in the assessment of neointimal thickness revealed remarkable similarity in both measurement data sets with clustering around the zero difference line and few outliers.

measurement of stent area. Furthermore, differences from the origin in the intercept of the lumen and neointimal areas correlation lines are due to slight differences in their measurements found throughout the samples, explanations for which were hypothesized within the paper.

Although Bland-Altman plots for the visualization of the method measurement differences were also constructed, their inclusion in the paper was decided against in the interests of space. As a matter of fact, Bland-Altman plots for all variables analyzed, besides stent areas, did not uncover any differences between methodologies examined in this study. The Bland-Altman plot developed for the evaluation of neointimal thickness is shown. As can be seen, the mean of the differences are very close to 0 for all parameter measures with few outliers. Furthermore, it is important to clarify that the Barlis article referred to by Ferrante et al. and plots therein are primarily concerned with optical coherence tomography interobserver and intraobserver measurement variability and not the contrast of heterogeneous measurement modalities.

David Wallace-Bradley, B.Sci
***Juan F. Granada, MD**

*Skirball Center for Cardiovascular Research
The Cardiovascular Research Foundation
8 Corporate Drive
Orangeburg, New York 10962
E-mail: jgranada@crf.org

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COMMENTARY

Care should be taken when interpreting data analysis from a small-patient series. In general, these reports are hypothesis-generating and lack the precision when compared to a much larger series. Definitive statements regarding small-patient series should be avoided unless full validation of the reported results have been achieved. The Bland-Altman plots describe a wider splay in the differences than noted by the authors; suggesting in larger samples that the correlations noted in this hypothesis-generating series may not be replicated.

Leslee J. Shaw, PhD
Associate Editor, *JACC: Cardiovascular Imaging*

Professor of Medicine, Emory University School of Medicine, Atlanta, Georgia

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